Herd immunity and pneumococcal conjugate vaccines

Kim Mulholland
Why should pneumococcal conjugate vaccines provide herd immunity?

• Impact on carriage has been seen in almost all studies:
  – ↓carriage of vaccine types
  – ↑carriage of non-vaccine types

• Herd effects depend on transmission patterns
USA - Rates of IPD caused by PCV7 serotypes among adults \( \geq 18 \) years-old, ABCs 1998-2009

- 2009 vs. baseline
  - 65+: -97% (96-98)
  - 50-64: -92% (89-94)
  - 18-49: -96% (94-97)

Moore, IDSA, 2009

CDC slides courtesy of C Whitney, M Moore, CDC
Rates of IPD caused by all serotypes among adults ≥18 years-old, ABCs 1998-2009

2009 vs. baseline
65+: -39% (-33, -44)
50-64: -15% (-5, -24)
18-49: -44% (-38, -62)

CDC slides courtesy of C Whitney, M Moore, CDC

Moore, IDSA, 2009
## Rates of IPD Caused by Serotype 19A among adults ≥18 years-old, ABCs 1998-2009

<table>
<thead>
<tr>
<th>Age, years</th>
<th>Percent change (95% CI)</th>
<th>Rate difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>65+</td>
<td>+157% (+81,+264)</td>
<td>3.5</td>
</tr>
<tr>
<td>50-64</td>
<td>+372% (+184,+684)</td>
<td>2.7</td>
</tr>
<tr>
<td>18-49</td>
<td>+251% (+138,+418)</td>
<td>.98</td>
</tr>
</tbody>
</table>

CDC slides courtesy of C Whitney, M Moore, CDC
Estimated IPD cases prevented among all ages, United States 2001-2009

280,000 cases & 19,000 deaths prevented

Pilishvili JID 2010 & CDC unpublished

CDC slides courtesy of C Whitney, M Moore, CDC
Rank order of IPD serotypes among Adults ≥65 years of age, 2009

CDC, unpublished, 2009

CDC slides courtesy of C Whitney, M Moore, CDC
Australia – Incidence of IPD, non-Indigenous, age < 2yrs

*Serotypes 6A, 9N, 19A

Courtesy Dr C Chiu, NCIRS
Australia – Incidence of IPD, non-Indigenous, age 5-65 yrs

*Serotypes 6A, 9N, 19A

Courtesy Dr C Chiu, NCIRS
Australia – Incidence of IPD, non-Indigenous, age >65 yrs

*Serotypes 6A, 9N, 19A

Courtesy Dr C Chiu, NCIRS
## Norway experience – IPD incidence

<table>
<thead>
<tr>
<th>Age</th>
<th>Pre-vaccine</th>
<th>Post-vaccine</th>
</tr>
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<tbody>
<tr>
<td>&lt;5 years</td>
<td>27</td>
<td>1.4</td>
</tr>
<tr>
<td>5-19</td>
<td>2</td>
<td>0.5</td>
</tr>
<tr>
<td>20-39</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>40-64</td>
<td>12</td>
<td>5</td>
</tr>
<tr>
<td>&gt;65</td>
<td>42</td>
<td>24</td>
</tr>
</tbody>
</table>

Vaccine 28 (2010) 2214–2221
Rates of IPD in infants under 90 days (USA)

JAMA 2006;295:1668-74
IPD in US infants under 90 days

JAMA 2006;295:1668-74
Young Infants Study 1 - *S. pneumoniae* isolates from blood or CSF

<table>
<thead>
<tr>
<th>Month</th>
<th>1st month</th>
<th>2nd month</th>
<th>3rd month</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>8</td>
<td>14</td>
<td>11</td>
</tr>
</tbody>
</table>

- Case fatality rate: 34%
- 17 cases CSF culture positive

- Serotype 2: 9
- Serotype 5: 9
- Serotype 7F: 2
- One each of 1, 6 (unk), 7(unk), 9L, 9V, 10, 12 (unk), 12F, 18F, 19F, 19A, 23F, 27, 33F, two unknown

Impact of PCV on rates of IPD due to strains non-susceptible to penicillin
Indirect effects arising from the impact of PCVs on carriage

• The bright side – herd immunity
• The dark side – serotype replacement
  – Wherever PCV’s introduced, carriage and disease due to non-vaccine types (NVT) ↑
Serotype replacement

- Theoretical risk → real impact in all settings
- Replacement = competition in carriage
- Industrialized countries
  - USA (after 9 years)
    - Strong impact in some settings (Alaska)
    - More important for immuno-compromised
    - Dominance of 19A
  - UK (after 3 years)
    - More rapid replacement
Invasive pneumococcal disease in Alaskan natives – under 2 years

JAMA 2007;297:1784-92
Pneumococcal meningitis cases in children under 5 in the UK by year

Australia – IPD rates by serotype, <2 yrs

Courtesy Dr C Chiu, NCIRS
What will happen in the developing world?

- The effectiveness (and the future) of pneumococcal vaccination in the developing world depends on:
  - Herd effects
  - Serotype replacement
Consider two scenarios...

• Scenario 1 –
  – 20% of young children carry Pnc
  – Carriage rare among older children and adults
  – Antibiotic use common

• Scenario 2 –
  – 90+% of children carry Pnc, often multiple types
  – Carriage common in older children and adults
Will positive herd effects be seen in developing countries?


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<tbody>
<tr>
<td>&lt; 5</td>
<td>35</td>
<td>16</td>
<td>15</td>
</tr>
<tr>
<td>5–14</td>
<td>15</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>≥15</td>
<td>58</td>
<td>50</td>
<td>69</td>
</tr>
<tr>
<td>Total</td>
<td>108</td>
<td>72</td>
<td>93</td>
</tr>
</tbody>
</table>

Non-vaccine types about half of under 5 cases, no increase
In adults vaccine type IPD decreased while non-vaccine type IPD increased

MJA 2008; 189: 43–46
Potential strategies to minimize the impact of replacement

• Keep using bigger and more expensive vaccines

• Use a softer schedule that will have less impact on carriage
  – 2+1 or 1+1 schedules show promise

• Rotate simpler, low valency vaccines

• Move to other vaccine approaches
Conclusions

• With pneumococcal conjugate vaccines, the impact on carriage has two opposing consequences:
  – Herd immunity $\rightarrow$ $\uparrow$ effectiveness
  – Serotype replacement $\rightarrow$ $\downarrow$ effectiveness

• Unless countries are empowered to monitor these effects and adjust their programs accordingly the global PCV program may fail.